REMARKS

The Office Action of January 30, 2008 presents the examination of claims 1-5. Claim 1 is amended to incorporate the features of claims 2-4, which are accordingly canceled. Claim 5 is amended to correct dependency.

Rejection under 35 USC § 112, second paragraph

Claim 5 stands rejected under 35 USC § 112, second paragraph, as allegedly being vague and indefinite. Applicants do not agree that claim 5 must recite any step of producing or isolating the hydrochloride (2), since such steps are recited in claim 1 from which claim 5 depends. Accordingly, this rejection should be withdrawn.

Rejection under 35 USC § 102

Claims 1-4 are rejected under 35 USC § 102(b) as being anticipated by Saji et al., US '372. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner asserts that example 1(d) of Saji discloses dissolution of the compound 101 (i.e. formula (1) in the present claim 1) in acetone and isopropanol containing 13.7% HCl.

However, the presently claimed invention is well distinguished from the cited Saji et al. reference; in particular in that only acetone is used as the solvent, and the amount of HCl used is substantially less than 13.7%. Accordingly, the instant rejection should be withdrawn.

Should the Examiner contemplate imposing a rejection for obviousness in view of Applicants' amendments of the claims, Applicants submit the following explanation of unobviousness of the present invention:

(i) Differences in the conditions in the process of preparation of the desired compound

It is true that the cited Saji et al. disclose a process for the preparation of the same compound as in the present invention, but as is mentioned in the present specification, the compound prepared by the method disclosed in Saji et al '372 has at least the problem of rather low purity of the compound, impairing its use in industrial processes.

In order to eliminate the defects in the process of Saji et al., the solvent to be used in the process of the present invention is acetone, while in Saji et al. a mixture of acetone and isopropanol is used. Also, the concentration of the aqueous hydrochloric acid is in the range of 2.8 - 5.0% in the present invention, while in Saji et al. 13.7 % isopropanol solution of hydrochloric acid is used. Applicants submit that these modifications of the process of Saji are not at all disclosed or suggested by the reference and therefore are not *prima facie* obvious from the disclosure of the reference.

ii) Superiority of the present invention to Saji et al.

As mentioned above, the process disclosed in Saji et al. has some problem in view of the production of the desired compound on industrial scale. According to the process of the present invention, owing to the differences in the kind of the solvent and the concentration of hydrochloric acid solution, the desired compound can be prepared in a high purity with high yield.

The Examiner should note that when the hydrochloride (2) as claimed in the present claims has once been obtained, it is very difficult, almost impossible, to purify it further by a conventional method, as there is no suitable solvent for it, and hence it is impossible to further purify the hydrochloride by a re-crystallizing technique, or by other known methods such as chromatography.

In order to use the compound (2) as a drug (its typical utility), it is required to have an extremely high purity for purposes of safety. If the product contains impurities or remaining solvents from the preparation procedure, these must be removed by purification. According to the process as disclosed in Saji et al., however, the obtained hydrochloride

product has remaining solvents, impurities, etc. and hence is not suitable for use as a drug.

However, according to the process of the present invention, the desired compound can be obtained in an extremely high purity and hence can be used as a drug without necessity of difficult purification methods.

In order to prove experimentally the superior effects of the present invention in comparison with the process of the cited Saji et al., comparative experiments have been done as shown in the attached Declaration by Mr. Bando.

As is clear from the results in Experiment 1 of Mr. Bando's Declaration, according to the method of the cited Saji et al. reference, the obtained imide compound hydrochloride has impurities in an amount of 0.22 % by weight and also a high amount (1.73 % by weight) of residual acetone from the solvent. On the other hand, when prepared according to the method of the present invention, the desired imide compound hydrochloride could be obtained in high purity, that is, having much less impurity content (0.04 % by weight) and also much less residual acetone (0.04 % by weight) in comparison with the product prepared by the method of *Saji* et al.

As is shown in Experiment 2 of Mr. Bando's Declaration as well as the present description, Example 14, particularly Table 1, when a solution of the free base of the specific compound as defined in the present claim 1 in acetone was added dropwise to an aqueous hydrochloric acid solution having a concentration in the range of 1.8 to 5.0 % by weight, the desired hydrochloride compound was obtained in high yield, with less impurities and less contamination with the solvent acetone.

It has never been taught or even suggested by the cited Saji et al. or any other prior art that one can obtain the desired hydrochloride compound (2) having such a high purity as by the method of the present invention.

Thus, the present invention has never been taught or even suggested by the cited Saji et al. and hence the present invention is well patentable over the cited Saji et al. '372.

Conclusion

Applicants submit that the present application well-describes and claims subject matter free of the prior art. Accordingly, the favorable actions of withdrawal of the standing rejections and allowance of the application are requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D., Reg. No. 36,623 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

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Respectfully submitted,

By _____

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